Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

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Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 1 of 5)
(Last updated December 10, 2015; last reviewed December 10, 2015)

Opportunistic Infections	Indication	Preferred	Alternative
***Pneumocystis* pneumonia (PCP)**	• CD4 count <200 cells/mm^3 **(AI)**, *or* • Oropharyngeal candidiasis **(AII)**, *or* • CD4 <14% **(BII)**, *or* • History of AIDS-defining illness **(BII)**, *or* • CD4 count >200 but <250 cells/mm^3 if monitoring CD4 cell count every 3 months is not possible **(BII)** **Note:** Patients who are receiving pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis **(AII)**.	• TMP-SMX[a] 1 double-strength (DS) PO daily **(AI)**, *or* • TMP-SMX[a] 1 single-strength (SS) daily **(AI)**	• TMP-SMX[a] 1 DS PO three times weekly **(BI)**, *or* • Dapsone[b] 100 mg PO daily or 50 mg PO BID **(BI)**, *or* • Dapsone[b] 50 mg PO daily + (pyrimethamine 50 mg + leucovorin 25 mg) PO weekly **(BI)**, *or* • (Dapsone[b] 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly **(BI)**; *or* • Aerosolized pentamidine 300 mg via Respigard II™ nebulizer every month **(BI)**, *or* • Atovaquone 1500 mg PO daily **(BI)**, *or* • (Atovaquone 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg) PO daily **(CIII)**
***Toxoplasma gondii* encephalitis**	• Toxoplasma IgG-positive patients with CD4 count <100 cells/µL **(AII)**; • Seronegative patients receiving PCP prophylaxis not active against toxoplasmosis should have toxoplasma serology retested if CD4 count decline to <100 cells/µL **(CIII)**. Prophylaxis should be initiated if seroconversion occurred **(AII)**. **Note:** All regimens recommended for primary prophylaxis against toxoplasmosis are also effective as PCP prophylaxis.	TMP-SMX[a] 1 DS PO daily **(AII)**	• TMP-SMX[a] 1 DS PO three times weekly **(BIII)**, *or* • TMP-SMX[a] 1 SS PO daily **(BIII)**, *or* • Dapsone[b] 50 mg PO daily + (pyrimethamine 50 mg + leucovorin 25 mg) PO weekly **(BI)**, *or* • (Dapsone[b] 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly **(BI)**; *or* • Atovaquone 1500 mg PO daily **(CIII)**; *or* • (Atovaquone 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg) PO daily **(CIII)**
***Mycobacterium tuberculosis* infection (TB)** (i.e., treatment of latent TB infection [LTBI])	• (+) screening test for LTBI[c], with no evidence of active TB, and no prior treatment for active TB or LTBI **(AI)**, *or* • Close contact with a person with infectious TB, with no evidence of active TB, regardless of screening test results **(AII)**.	• (INH 300 mg + pyridoxine 25 mg) PO daily x 9 months **(AII)**, *or* • INH 900 mg PO BIW (by DOT) + pyridoxine 25 mg PO daily x 9 months **(BII)**.	• Rifampin 600 mg PO daily x 4 months **(BIII)**, *or* • Rifabutin (dose adjusted based on concomitant ART)[d] x 4 months **(BIII)**. For persons exposed to drug-resistant TB, select anti-TB drugs after consultation with experts or public health authorities **(AII)**.
Disseminated *Mycobacterium avium* complex (MAC) disease	CD4 count <50 cells/µL—after ruling out active disseminated MAC disease based on clinical assessment **(AI)**.	• Azithromycin 1200 mg PO once weekly **(AI)**, *or* • Clarithromycin 500 mg PO BID **(AI)**, *or* • Azithromycin 600 mg PO twice weekly **(BIII)**	Rifabutin (dose adjusted based on concomitant ART)[d] **(BI)**; rule out active TB before starting rifabutin

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***Streptococcus pneumoniae* infection**	For individuals who have not received any pneumococcal vaccine, regardless of CD4 count, followed by:	PCV13 0.5 mL IM x 1 **(AI)**.	PPV23 0.5 mL IM or SQ x 1 **(BII)**
	• if CD4 count ≥200 cells/μL	PPV23 0.5 mL IM or SQ at least 8 weeks after the PCV13 vaccine **(AII)**.	
	• if CD4 count <200 cells/μL	PPV23 can be offered at least 8 weeks after receiving PCV13 **(CIII)** or can wait until CD4 count increased to ≥200 cells/μL **(BIII)**.	
	For individuals who have previously received PPV23	One dose of PCV13 should be given at least 1 year after the last receipt of PPV23 **(AII)**.	
	Re-vaccination • If age 19–64 years and ≥5 years since the first PPV23 dose • If age ≥65 years, and if ≥5 years since the previous PPV23 dose	• PPV23 0.5 mL IM or SQ x 1 **(BIII)** • PPV23 0.5 mL IM or SQ x 1 **(BIII)**	
Influenza A and B virus infection	All HIV-infected patients **(AIII)**	Inactivated influenza vaccine annually (per recommendation for the season) **(AIII)** Live-attenuated influenza vaccine is **contraindicated** in HIV-infected patients **(AIII)**.	
Syphilis	• For individuals exposed to a sex partner with a diagnosis of primary, secondary, or early latent syphilis within past 90 days **(AII)**, *or* • For individuals exposed to a sex partner >90 days before syphilis diagnosis in the partner, if serologic test results are not available immediately and the opportunity for follow-up is uncertain **(AIII)**	Benzathine penicillin G 2.4 million units IM for 1 dose **(AII)**	*For penicillin-allergic patients:* • Doxycycline 100 mg PO BID for 14 days **(BII)**, *or* • Ceftriaxone 1 g IM or IV daily for 8–10 days **(BII)**, *or* • Azithromycin 2 g PO for 1 dose **(BII)** – **not recommended** for MSM or pregnant women **(AII)**
***Histoplasma capsulatum* infection**	CD4 count ≤150 cells/μL and at high risk because of occupational exposure or live in a community with a hyperendemic rate of histoplasmosis (>10 cases/100 patient-years) **(BI)**	Itraconazole 200 mg PO daily **(BI)**	

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Opportunistic Infections	Indication	Preferred	Alternative
Coccidioidomycosis	A new positive IgM or IgG serologic test in patients who live in a disease-endemic area and with CD4 count <250 cells/μL **(BIII)**	Fluconazole 400 mg PO daily **(BIII)**	
Varicella-zoster virus (VZV) infection	Pre-exposure prevention: Patients with CD4 counts ≥200 cells/μL who have not been vaccinated, have no history of varicella or herpes zoster, or who are seronegative for VZV **(CIII)** **Note:** Routine VZV serologic testing in HIV-infected adults and adolescents is not recommended. Post-exposure prevention: **(AIII)** Close contact with a person with chickenpox or herpes zoster; and is susceptible (i.e., no history of vaccination or of either condition, or known to be VZV seronegative)	Pre-exposure prevention: Primary varicella vaccination (Varivax™), 2 doses (0.5 mL SQ each) administered 3 months apart **(CIII)**. If vaccination results in disease because of vaccine virus, treatment with acyclovir is recommended **(AIII)**. Post-exposure prevention: Varicella-zoster immune globulin (VariZIG™) 125 international units per 10 kg (maximum 625 international units) IM, administered as soon as possible and within 10 days after exposure **(AIII)** **Note:** VariZIG is exclusively distributed by FFF Enterprises at 800-843-7477. Individuals receiving monthly high-dose IVIG (>400 mg/kg) are likely to be protected if the last dose of IVIG was administered <3 weeks before exposure.	Pre-exposure prevention: VZV-susceptible household contacts of susceptible HIV-infected persons should be vaccinated to prevent potential transmission of VZV to their HIV-infected contacts **(BIII)**. Alternative post-exposure prevention: • Acyclovir 800 mg PO 5 x/day for 5–7 days **(BIII)**, *or* • Valacyclovir 1 g PO TID for 5–7 days **(BIII)** These alternatives have not been studied in the HIV population. If antiviral therapy is used, varicella vaccines should not be given until at least 72 hours after the last dose of the antiviral drug.
Human Papillomavirus (HPV) infection	Females aged 13–26 years **(BIII)**	• HPV quadrivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 **(BIII)**, *or* • HPV bivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 **(BIII)**, *or* • HPV 9-valent vaccine 0.5 mL IM at months 0, 1–2, and 6 **(BIII)**	
	Males aged 13–26 years **(BIII)**	• HPV quadrivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 **(BIII)**, *or* • HPV 9-valent vaccine 0.5 mL IM at months 0, 1–2, and 6 **(BIII)**	

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Opportunistic Infections	Indication	Preferred	Alternative
Hepatitis A virus (HAV) infection	HAV-susceptible patients with chronic liver disease, or who are injection-drug users, or MSM **(AII)**.	Hepatitis A vaccine 1 mL IM x 2 doses at 0 and 6–12 months **(AII)**. IgG antibody response should be assessed 1 month after vaccination; non-responders should be revaccinated when CD4 count >200 cells/μL. **(BIII)**.	For patients susceptible to both HAV and hepatitis B virus (HBV) infection (see below): Combined HAV and HBV vaccine (Twinrix®), 1 mL IM as a 3-dose (0, 1, and 6 months) or 4-dose series (days 0, 7, 21 to 30, and 12 months) **(AII)**
Hepatitis B virus (HBV) infection	• Patients without chronic HBV or without immunity to HBV (i.e., anti-HBs <10 international units/mL) **(AII)** • Patients with isolated anti-HBc and negative HBV DNA **(BII)** • Early vaccination is recommended before CD4 count falls below 350 cells/μL **(AII)**. • However, in patients with low CD4 cell counts, vaccination should not be deferred until CD4 count reaches >350 cells/μL, because some patients with CD4 counts <200 cells/μL do respond to vaccination **(AII)**.	• HBV vaccine IM (Engerix-B 20 μg/mL or Recombivax HB 10 μg/mL), 0, 1, and 6 months **(AII)**, *or* • HBV vaccine IM (Engerix-B 40 μg/mL or Recombivax HB 20 μg/mL) 0, 1, 2 and 6 months **(BI)**, *or* • Combined HAV and HBV vaccine (Twinrix®), 1 mL IM as a 3-dose (0, 1, and 6 months) or 4-dose series (days 0, 7, 21 to 30, and 12 months) **(AII)** Anti-HBs should be obtained 1 month after completion of the vaccine series. Patients with anti-HBs <10 international units/mL at 1 month are considered non-responders **(BIII)**.	Some experts recommend vaccinating with 40-μg doses of either HBV vaccine **(CIII)**.
	Vaccine Non-Responders: • Anti-HBs <10 international units/mL 1 month after vaccination series • For patients with low CD4 counts at time of first vaccine series, some experts might delay re-vaccination until after a sustained increase in CD4 count with ART **(CIII)**.	Re-vaccinate with a second vaccine series **(BIII)**	• HBV vaccine IM (Engerix-B 40 μg/mL or Recombivax HB 20 μg/mL), 0, 1, 2 and 6 months **(BI)**.
Malaria	Travel to disease-endemic area	Recommendations are the same for HIV-infected and HIV-uninfected patients. Recommendations are based on region of travel, malaria risks, and drug susceptibility in the region. Refer to the following website for the most recent recommendations based on region and drug susceptibility: http://www.cdc.gov/malaria/.	

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Opportunistic Infections	Indication	Preferred	Alternative
Penicilliosis	Patients with CD4 cell counts <100 cells/μL who live or stay for a long period in rural areas in northern Thailand, Vietnam, or Southern China **(BI)**	Itraconazole 200 mg once daily **(BI)**	Fluconazole 400 mg PO once weekly **(BII)**

Key to Acronyms: anti-HBc = hepatitis B core antibody; anti-HBs = hepatitis B surface antibody; ART = antiretroviral therapy; BID = twice daily; BIW = twice a week; CD4 = CD4 T lymphocyte cell; DOT = directly observed therapy; DS = double strength; HAV = hepatitis A virus; HBV = hepatitis B virus; HPV = human papillomavirus; IgG = immunoglobulin G; IgM = immunoglobulin M; IM = intramuscular; INH = isoniazid; IV= intravenously; IVIG = intravenous immunoglobulin; LTBI = latent tuberculosis infection; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis* pneumonia; PCV13 = 13-valent pneumococcal conjugate vaccine; PO = orally; PPV23 = 23-valent pneumococcal polysaccharides vaccine; SQ = subcutaneous; SS = single strength; TB = tuberculosis; TMP-SMX = Trimethoprim-sulfamethoxazole; VZV = varicella zoster virus

[a] TMP-SMX DS once daily also confers protection against toxoplasmosis and many respiratory bacterial infections; lower dose also likely confers protection

[b] Patients should be tested for glucose-6-phosphate dehydrogenase (G6PD) before administration of dapsone or primaquine. Alternative agent should be used in patients found to have G6PD deficiency

[c] Screening tests for LTBI include tuberculin skin test (TST) or interferon-gamma release assays (IGRA)

[d] Refer to Table 5 for dosing recommendation

Evidence Rating:

Strength of Recommendation:

A: Strong recommendation for the statement

B: Moderate recommendation for the statement

C: Optional recommendation for the statement

Quality of Evidence for the Recommendation:

I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints

II: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes

III: Expert opinion

In cases where there are no data for the prevention or treatment of an OI based on studies conducted in HIV-infected populations, but data derived from HIV-uninfected patients exist that can plausibly guide management decisions for patients with HIV/AIDS, the data will be rated as III but will be assigned recommendations of A, B, C depending on the strength of recommendation.